95. (new) The method of Claim 12, further comprising the step of contacting said cell with a concentration of inducer which induces transcription of said antisense nucleic acid to a sublethal level.

96. (new) The method of Claim 12, wherein growth inhibition is measured by monitoring optical density of a culture medium.

97. (new) The method of Claim 12, wherein said gene product is a polypeptide.

98. (new) The method of Claim 97, wherein said polypeptide is selected from the group consisting of 5021, 5283, 10251, 10689, 10969, 11370, 11955, 12600, 13518 and 13703.

99. (new) The method of Claim 12, wherein said nucleic acid encoding said gene product is selected from the group consisting of 3966, 4228, 6154, 6592, 6872, 7273, 7857, 8502, 9420 and 9605.

REMARKS

Claim 31 has been amended to broaden its scope. New claims 45-84, which are dependent on claim 31, and claims 85-99, which are dependent on claim 12, have also been added. Each claim includes a set of specific SEQ ID NOs corresponding to the *yphC* antisense nucleic acids, a set of specific SEQ ID NOs corresponding to the *yphC* genes, or a set of specific SEQ ID NOs corresponding to the YphC polypeptides. Applicants agree to withdrawal of claims 1-11, 13-30 and 32-44 from further consideration in the instant application without prejudice or disclaimer but reserve their right to prosecute these claims in future divisional or other continuing applications. Accordingly, claims 12, 31 and 45-99 are currently pending.

SUPPORT FOR CLAIM AMENDMENTS

Support for the broadening amendments to claims 12 and 31 appear in the specification on page 148, lines 13-20 and throughout Example 8. Support for new claims 45-56 and 85-99 can be found on pages 46-49 and throughout the application. Support for new claims 57-84 can be found beginning on page 75, line 22 through page 81, line 2. Additional support specific for claims 69 and 70 is present in Table VIIA. Accordingly, no new matter has been added to this application.

SEQUENCE ELECTION REQUIREMENT

Applicants respectfully traverse the sequence election requirement, which limits examination of the elected claim group with respect to one sequence. Although Applicants provisionally elect the polypeptide sequence of SEQ ID NO: 12600 for examination, Applicants maintain that the current law permits the examination of more than one sequence when each of the sequences is embraced by a generic linking claim. No searching burden is created since it is sufficient for patentability to simply verify the novelty of Applicants' discovery that *yphC* is an essential microbial gene. The Court of Appeals for the Federal Circuit has recognized that Applicant is entitled to the examination of a generic claim encompassing a number of polynucleotides or polypeptides when the application provides a representative number of related sequences which fall within the scope of the generic claim. *The Regents of the Univ. of Calif. v. Eli Lilly & Co.*, 119 F.3d 1559, 1569 (Fed. Cir. 1997). As discussed in more detail below, Applicants have discovered the essentiality of the *yphC* gene and its encoded polypeptide using a number of antisense nucleic acids complementary to at least a portion of the *yphC* gene. Applicants have provided the sequences of the antisense nucleic acids, as well as the sequences of the *yphC* genes from several organisms and the YphC polypeptides from several organisms. Knowledge of the essentiality of the *yphC* gene and its encoded polypeptide allow the antisense nucleic acids, *yphC* genes, and YphC polypeptides to be used in methods for screening candidate compounds for the ability to reduce cellular proliferation. Applicants have provided a linking claim which encompasses the use of the antisense nucleic acids, *yphC* genes and yphC polypeptides provided in the application in such screening methods. This linking claim is supported by a representative number of *yphC* antisense and coding nucleic acids as well a representative number of YphC polypeptides. As discussed in more detail below, Applicants maintain that the relationship between the sequences provided by the Applicant entitles the Applicant to have the linking claim and the claims dependent thereon which recite more than one sequence examined together in the present application. Accordingly, Applicants elect the single invention relating to *yphC* for examination and maintain that this single invention encompasses more than one sequence as discussed more fully below.

With respect to the single invention relating to *yphC*, as described in the specification, Applicants have discovered that the *yphC* gene and its encoded polypeptide are essential for microbial proliferation. As described in the specification, Applicants discovered the essentiality

of the *yphC* gene and its encoded polypeptide by demonstrating that the expression of antisense nucleic acids complementary to the *yphC* gene inhibited proliferation. Thus, the *yphC* gene and its encoded polypeptide are useful, for example, in the claimed methods in which an antisense nucleic acid is used to generate sensitized cells for use in methods for screening compounds for the ability to reduce cellular proliferation. Each of the pending claims include sequences which relate to one or more of the following: (1) antisense nucleic acids complementary to at least a portion of the *yphC* gene from either *Staphylococcus aureus* or *Enterococcus faecalis*; (2) the *yphC* gene from different organisms; and (3) YphC polypeptides from different organisms.

In the specification of the present application, Applicants have provided the sequences of several antisense nucleic acids which are complementary to the *Staphylococcus aureus* and *Enterococcus faecalis yphC* genes, the sequence of the y*phC* gene from several organisms and the sequences of the YphC polypeptides from several organisms. In particular, Applicants have provided the antisense nucleic acids of SEQ ID NOs: 1390, 1463, 1845, 2782 and 3283, which are complementary to the *Staphylococcus aureus yphC* gene, and the antisense nucleic acid of SEQ ID NO: 521, which is complementary to the *Enterococcus faecalis yphC* gene; the *Staphylococcus aureus yphC* gene of SEQ ID NO: 4228, the *Enterococcus faecalis yphC* gene of SEQ ID NO: 6592, as well as the *yphC* gene from several different organisms having SEQ ID NOs: 3966, 6154, 6872, 7273, 7857, 8502, 9420 and 9605; and the YphC polypeptides from several different organisms of SEQ ID NOs: 5021, 5283, 10251, 10689, 10969, 11370, 11955, 12600, 13518 and 13703.

Applicants would like to note that in the other applications being examined by the United States Patent Office which relate to similar subject matter, Applicants have been successful in obtaining the examination of claims relating to a particular antisense nucleic acid, its complementary gene, and the polypeptide encoded by the complementary gene from a single organism. In those cases as well as the instant application, a connection exists between the antisense nucleic acid, the complementary gene, and the polypeptide because of their biological interrelationship. Applicants note that the antisense nucleic acid is complementary to at least a portion of the gene and that the gene in turn encodes the polypeptide. Applicants also note they have discovered that expression of the antisense nucleic acids inhibits cellular proliferation, thereby indicating that the gene and its encoded protein are essential. In view of this essentiality,

the antisense nucleic acid, the gene and the polypeptide can be used in methods for identifying compounds which inhibit proliferation. In light of the aforementioned biological interrelationships, Applicants maintain that the antisense, sense and polypeptides as related to the *yphC* gene are sufficiently related to be examined together since all of the claims stem from the identification of an essential gene using the antisense nucleic acids.

In addition to the above biological interrelationship between antisense, coding and polypeptide sequences, Applicants would like to emphasize the fact that the *yphC* genes encode essential YphC polypeptides which share sequence homology with each other. In particular, each of SEQ ID NOs: 5021, 5283, 10251, 10689, 10969, 11370, 11955, 12600, 13518 and 13703 correspond to YphC polypeptides from several different organisms. Each of these homologous polypeptides share significant regions of sequence identity. As such, Applicants maintain that each of the sequences corresponding to YphC polypeptides are sufficiently related to be examined together.

In light of each of the foregoing arguments, Applicants respectfully submit that claims reciting each of the YphC polypeptides, the genes which encode them, and antisense nucleic acids complementary to the *yphC* genes can be examined together.

ALTERNATIVE ELECTION CORRESPONDING TO YphC POLYPEPTIDES

In the argument set out above, Applicants have noted the interrelationship among YphC polypeptides, the gene encoding YphC, and nucleic acid sequences complementary thereto. Applicants have also described the relationship between the homologous YphC polypeptides. In addition to the foregoing, Applicants would like to particularly point out that only a search for the essentiality of the YphC polypeptide would be required to examine claims drawn to this set of sequences. Patentability does not require novelty of these sequences. Accordingly, in the event that the Examiner finds the above argument unpersuasive, Applicants request that the claims of Group VII be examined with respect to the above polypeptide sequences which correspond to YphC (i.e. SEQ ID NOs: 5021, 5283, 10251, 10689, 10969, 11370, 11955, 12600, 13518 and 13703). As discussed above, Applicants maintain that all of these sequences should be examined together because they all relate to YphC polypeptides which are useful in the claimed methods.

ALTERNATIVE ELECTION OF *yphC* NUCLEIC ACIDS AND POLYPEPTIDES FROM STAPHYLOCOCCUS AUREUS

In the arguments set out above, Applicants have shown the biological interrelationship between nucleic acids and polypeptides related to the essential *yphC* gene. Applicants have also shown that the polypeptides recited in each of the claims share significant sequence identity and can be searched based on the essentiality of YphC. However, in the event that the Examiner finds the above arguments unpersuasive, Applicants request the claims of Group VII be examined with respect to SEQ ID NO: 4228 (*yphC* from *Staphylococcus aureus*), SEQ ID NOs: 1390, 1463, 1845, 2782 and 3283 (antisense nucleic acids complementary to at least portions of *yphC* from *S. aureus*) and SEQ ID NO: 12600 (YphC from *S. aureus*). As discussed above, Applicants maintain that all of these sequences should be examined together because they relate to the *Staphylococcus aureus yphC* gene, antisense nucleic acids complementary to at least a portion thereof, or the polypeptide encoded thereby.

ALTERNATIVE ELECTION OF YphC FROM STAPHYLOCOCCUS AUREUS

In the event that the Examiner finds each of the above arguments unpersuasive, Applicants request that the claims of Group VII be examined with respect to the polypeptide of SEQ ID NO: 12600. In the event that the Examiner limits examination to SEQ ID NO: 12600, Applicant notes that the pending claims reciting this particular SEQ ID NO are present in dependent claims 58-70 as well as dependent claim 98 .

CONCLUSION

Applicants maintain that the claimed sequences are so related as to permit examination of the antisense and sense nucleic acids as well as the polypeptide for YphC in a single application because each of the foregoing sequences relates to the discovery that the *yphC* gene encodes a gene product required for proliferation.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: Oct. 22, 2002

By: Daniel Hart

Daniel Hart
Registration No. 40,637
Attorney of Record
Customer No. 20,995
(619) 235-8550

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS

12. (Amended) A method for **[identifying a compound which reduces the activity or level of a gene product required for proliferation of a cell, wherein the activity or expression of said gene product is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795, said method]** screening a candidate compound for the ability to reduce cellular proliferation comprising the steps of:

(a) providing a sublethal level of an antisense nucleic acid **[comprising a nucleotide sequence complementary to a nucleic acid comprising a nucleotide sequence encoding a said gene product in a cell to reduce thereby reducing the activity or amount of said gene product in said cell so as to produce, thereby producing a sensitized cell;]** complementary to at least a portion of a nucleic acid encoding a gene product in a cell to reduce the activity or amount of said gene product in said cell, thereby producing a sensitized cell, wherein said gene product is a gene product whose activity or amount is reduced by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 521, 1390, 1463, 1845, 2782 and 3283;

(b) contacting said sensitized cell with a compound; and

(c) determining the degree to which said compound inhibits proliferation of said sensitized cell relative to a **[cell which does not contain said antisense nucleic acid]** nonsensitized cell.

31. (Amended) A method for **[identifying a compound which reduces the activity or level of a gene product required for proliferation of a cell]** screening a candidate compound for the ability to reduce cellular proliferation comprising:

(a) providing a sublethal level of an antisense nucleic acid complementary to at least a portion of a nucleic acid encoding **[said]** a gene product in a cell to reduce the activity or amount of said gene product in said cell, thereby producing a sensitized cell, wherein said gene product is selected from the group consisting of **[a gene product having having at least 70% nucleic acid identity as determined using BLASTN**

version 2.0 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 8-3795,] a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs: **[8-3795]** 521, 1390, 1463, 1845, 2782 and 3283, a gene product having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: **[8-3795]** 521, 1390, 1463, 1845, 2782 and 3283, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: **[8-3795]** 521, 1390, 1463, 1845, 2782 and 3283 under stringent conditions, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: **[8-3795]** 521, 1390, 1463, 1845, 2782 and 3283 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid selected from the group consisting of SEQ ID NOs: **[8-3795]** 521, 1390, 1463, 1845, 2782 and 3283;

(b) contacting said sensitized cell with a compound; and

(c) determining the degree to which said compound inhibits the growth of said sensitized cell relative to **[a cell which does not contain said antisense nucleic acid]** a nonsensitized cell.